UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/357,013	08/05/99	KNUTZON	D CGAB-210-USA

HM22/1012

MICHAEL R WARD
LIMBACH & LIMBACH
2001 FERRY BUILDING
SAN FRANCISCO CA 94111

EXAMINER	
NASHED,N	
ART UNIT	**PAPER NUMBER**
1652	15

DATE MAILED: 10/12/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/367,013	Applicant(s) Knutzon et al.
	Examiner Nashaat T. Nashed	Art Unit 1652

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 2, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *65-188* is/are pending in the application.

4a) Of the above, claim(s) *67-92, 95-98, 101-186, and 188* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *65, 66, 93, 94, 99, 100, and 187* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

Applicant's election without traverse of Group I, claims 65, 66, 94, 99, 100, and 18 acknowledged. Also, applicants elected stearidonic acid without traverse for initial prosecution.

The drawings are objected to because of the defects noted on the attached PTO-498. Correction is required.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicants attention is directed tp page 61, lines 8-16 wherein three nucleic sequences are not identified by sequence identification numbers.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

The use of the trademark ISOMIL®, SIMILAC®, and OXEPA™ have been noted in this application, see pages 70-74 and 92. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 65, 66, 94, 99, 100, and 187 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6-10 and 15 of U.S. Patent No. 6,136,574 ('574). Although the conflicting claims are not identical, they are not patentably distinct from each other. Claim 65 and its dependent claims 66, 93 and 94 as well as claim 187 are drawn to a method of introducing desaturation in fatty acids to form stearidonic acid using a microbial cell such as yeast transformed with a nucleic acid sequence encoding a polypeptide wherein in the polypeptide comprises a sequence selected from the group consisting of residues 50-53, 39-43, 172-176, 204-213, and 390-402 of SEQ ID NO: 2. Claim 6 the '572 patent is limited to a method of making stearidonic acid comprising the culturing of a recombinant host cell comprising a Δ-6-desaturase from *Mortierella alpina*. Claim 15 of '572 patent is drawn to a method of making stearidonic acid comprising the culturing of a recombinant host eukaryotic cell comprising a Δ-6-desaturase from *Mortierella alpina*. Both methods of claims are specific embodiment of the claimed method in the instant application. Claims 99 and 100 are included in this rejection because they are drawn to presumably a triglycerides comprising stearidonic acid obtained from the microbial cell used in the method of making stearidonic acid of claim 65.

Claims 65, 66, 94, 99, 100, and 187 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 11 of U.S. Patent No. 6,075,183 ('183). Although the conflicting claims are not identical, they are not patentably distinct from each other. Claim 65 and its dependent claims 66, 93 and 94 as well as claim 187 are drawn to a method of introducing desaturation in fatty acids to form stearidonic acid using a microbial cell such as yeast transformed with a nucleic acid sequence encoding a polypeptide wherein in the polypeptide comprises a sequence selected from the group consisting of residues 50-53, 39-43, 172-176, 204-213, and 390-402 of SEQ ID NO: 2. Claim 11 the '183 patent is drawn to a microbial or plant host cell transformed with at least one nucleic acid sequence selected from a nucleic acid encoding the amino acid sequence of SEQ ID NO: 2 and 4. Since unsaturated fatty acid are recommended additive for healthy human diet, it would be obvious to one of ordinary skill in the art to use the microbial cell claimed '183 patent in a method to make long chain unsaturated fatty acid.

Claims 65, 66, 94, 99, 100, and 187 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-20 and 26-30 of U.S. Patent No. 5,968, 809 ('809). Although the conflicting claims are not identical, they are not patentably distinct from each other. Claim 65 and its dependent

claims 66, 93 and 94 as well as claim 187 are drawn to a method of introducing desaturation in fatty acids to form stearidonic acid using a microbial cell such as yeast transformed with a nucleic acid sequence encoding a polypeptide wherein in the polypeptide comprises a sequence selected from the group consisting of residues 50-53, 39-43, 172-176, 204-213, and 390-402 of SEQ ID NO: 2. Claims 12-20 and 26-30 the '809 patent are drawn to a recombinant host cell including yeast cell transformed with at least one nucleic acid sequence selected from a nucleic acid encoding the amino acid sequence of SEQ ID NO: 2 and 4. Since unsaturated fatty acid are recommended additive for healthy human diet, it would be obvious to one of ordinary skill in the art to use the host cell claimed '809 patent in a method to make long chain unsaturated fatty acid.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 65, 66, 93, 94, 99, 100, and 187 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 65, 66, 93, 94, 99, 100, and 187 are directed to a method utilizing a recombinant microbial cell transformed with all possible DNAs encoding a polypeptide wherein the sequence of the polypeptide comprises a sequence selected from the group consisting of residues 50-53, 39-43, 172-176, 204-213, and 390-402 of SEQ ID NO: 2. The specification, however, only provides two representative species from *Mortierella alpina* encoding two different enzymatic activities which are Δ-6-desaturase of SEQ ID NO: 2 and Δ-12-desaturase of SEQ ID NO: 4. It should be noted that the specification discloses several nucleic acid fragments encoding polypeptides comprising said fragments, but no function is indicated in the specification. In addition, said fragments are found in many proteins that have no Δ-6-desaturase or Δ-12-desaturase activities. The fragments are very small and the specification does not indicates that the amino acid sequences of those specific residues are required for a specific enzymatic activities. There is no disclosure of any particular structure to function/activity relationship in the two single disclosed species. The specification also fails to describe additional representative species of these DNAs by any identifying structural characteristics or properties other than the activities of encoding Δ-6-desaturase and Δ-12-desaturase, for which no predictability

of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Claims 65, 66, 93, 94, 99, 100, and 187 rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to methods of a lipid fraction enriched in stearidonic acid using yeast transformed with the nucleic acid sequences encoding Δ-6-desaturase of SEQ ID NO: 2 and Δ-12-desaturase of SEQ ID NO: 4 from *Mortierella alpina*. The specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. The claims are broader than the enablement provided by the disclosure with regard to all possible polypeptides comprising any of the small peptide fragments corresponding to residues 50-53, 39-43, 172-176, 204-213, and 390-402 of SEQ ID NO: 2. Factors to be considered in determining whether undue experimentation is required, are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses a general method of obtaining any modified long chain fatty acid using any microbial cell transformed with any nucleic acid encoding any polypeptide comprises any of the small peptide fragments corresponding to residues 50-53, 39-43, 172-176, 204-213, and 390-402 of SEQ ID NO: 2 from any biological source and having any enzymatic or non-enzymatic activities. Claim 99 and 100 are drawn a method of making "oil or fraction thereof", presumably a triglyceride comprising stearidonic acid moiety and the product of the method using a cell transformed with a nucleic acid encoding any protein comprising any of residues 50-53, 39-43, 172-176, 204-213, and 390-402 of SEQ ID NO: 2 from any biological source and having any enzymatic or non-enzymatic activities. The specification provides guidance and examples in the form of an assay to isolate and characterize the nucleic acid encoding Δ-6-desaturase of SEQ ID NO: 2 and Δ-12-desaturase of SEQ ID NO: 4 from *Mortierella alpina* and their use in obtaining unsaturated fatty acid from a culture of microorganism (see examples 1-8) and isolation and determining the amount of each unsaturated fatty acid in a lipid fraction. While molecular biological techniques and genetic manipulation to make the transformed microbial cell are known in the prior art and the skill of the artisan are well developed, knowledge regarding the function of a protein from any biological source comprising any of the small peptide fragments corresponding to residues 50-53, 39-43, 172-176, 204-213, and 390-402 of SEQ ID NO: 2 and their use is lacking. It is

noted that examples 9-11 disclose various nucleic acid sequences encoding polypeptides that have no specific function, and that proteins comprising any of the peptide fragments corresponding to residues 50-53, 39-43, 172-176, 204-213, and 390-402 of SEQ ID NO: 2 can have any function. It should be noted, while the application teaches the use of microorganism to make lipid fraction enriched in unsaturated fatty acids including stearidonic acid, it does not provide any teaching on how the stearidonic acid formed by the action of Δ-6 and Δ-12 desaturase be isolated, purified or prevent its esterification to triglycerides (claim 66); or enhance its esterification to triglycerides (claim 100). Thus, searching for a nucleic acid sequence encoding a polypeptide comprising any of the peptide fragments corresponding to residues 50-53, 39-43, 172-176, 204-213, and 390-402 of SEQ ID NO: 2 or developing a method of making triglycerides from stearidonic acid is well outside the realm of routine experimentation and predictability in the art of success is extremely low. The amount of experimentation to identify a nucleic acid encoding a polypeptide comprising one of the small fragments from any biological source, identify its function(s) and use it to modify fatty acids, and isolating the genes encoding the enzymes required for the esterification of stearidonic acid to triglycerides is enormous. Since routine experimentation in the art does not include screening vast numbers of genomic, cDNA or manmade DNA libraries, identifying a function of a protein product encoded by a nucleic acid isolated from said libraries, and develop a method to modify fatty acids which include any chemical transformation to any fatty acids including esterification, amidation, epoxidation and oxidative cleavage of the carbon chain of any fatty acids, where the expectation of obtaining the desired modified fatty acid is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the biological source, the desired modification to fatty acids, the chemical function of the protein comprising one or more of the small polypeptide from SEQ ID NO: 2, and the genes needed to convert stearidonic acid to triglycerides. Without such a guidance, the experimentation left to those skilled in the art is undue.

Claims 65, 66, 93, 94, 99, 100, and 187 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

(a) the phrase "altering long chain fatty acid" in claims 65 and 187 is render the claim indefinite. The word long is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Also, the word "altering" is not define by the claim and the specification does not define the word. For examination purposes only, the phrase is taken to mean any chemical modification including desaturation,

epoxidation, esterification, elongation of the fatty acid chain, amidation to any fatty acid having more than two carbon atoms.

(b) the phrase "oil or fraction thereof" in claims 99 and 100 renders the claims indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. While the word "oil" is taken to mean a fat or triglycerides comprising stearidonic acid moiety for examination purposes, a meaning for "fraction thereof" could not be interpreted in any chemical sense.

(c) Claims 66, 93, and 94 are included in this rejection and do not cure the deficiencies of the claims from which they depend.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claim 100 is rejected under 35 U.S.C. § 102(e) as being anticipated by [Horrobin *et al.* U. S. Patent 5,670,540 (540).

The 540 patent teaches chemical and enzymatic method of making fat from fatty acids including stearidonic acid, see the entire document. Claims drawn to di- and triglyceride compositions comprising a unsaturated fatty acids including stearidonic acid are claimed, see claim 2, and 13. Although the patent does not teach the specific method of claim 99, the patent teach making an oil (mixture of mono-, di- and triglyceride) comprising fatty acid moiety of unsaturated fatty acids such as stearidonic acid. Applicants have the burden of distinguishing their invention from that of the prior art.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is (703) 305-6586. The examiner can normally be reached Monday, Tuesday, Thursday and Friday from 9:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (703) 308-3804. The fax phone number for this Group is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nashaat T. Nashed, Ph. D.
Primary Examiner